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CHILLS IN TYPHOID FEVER.

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The attention of clinicians has been particularly called within recent years to the occurrence of extreme rigors associated with typhoid fever, either in the regular course of the disease or in some of its more serious complications. In Southern latitudes, especially, where the presence of chills in various fevers is apt to be ascribed to the growth in the blood of the malarial parasites, the exhibition of rigors in typhoid fever is usually considered to be due to a combination of intermittent and enteric fever, and the suspicion always exists that the sudden rise and fall in temperature is not due to the typhoid lesions but to the plasmodium malariae.

A number of cases of the combination of malaria and typhoid have been reported in the Medical and Surgical History of the War of the Rebellion, where the soldiers stationed in southern camps under unhygienic conditions contracted both diseases. For a number of years the occurrence of these two diseases in combination was a subject for great dispute, and the question was only finally settled after the outbreak of the Spanish-American war, when soldiers returning from the Philippines were found to have large numbers of malarial parasites in the circulating blood, and to have as well the clinical symptoms of typhoid fever, including a positive Widal reaction, which persisted after the disappearance of the parasites from the blood after the administration of quinine.

The following case which occurred in the Medical Wards of the Johns Hopkins Hospital in the service of Dr. Osler, which by his permission is here reported, represents a combination of symptoms which for the period of the entire stay of the patient in the hospital was looked upon with suspicion as being a combination of typhoid and malaria, but which during life to all apparent observations was absolutely negative for malaria and which at autopsy showed positive evidence of the lesions of typhoid fever.

CASE: Daniel Ryan, æt. 40, white, painter by occupation, admitted to the Johns Hopkins Hospital, March 5th, 1899, complaining of stomach trouble and rheumatism. Family history negative for constitutional diseases.

PERSONAL HISTORY: Smallpox at 10 during the Chicago epidemic, no history of malaria at any time; rheumatism at 22, beginning in the

joints of both feet which were swollen and painful, tender to the touch. Both knees were then involved, then hips, hands and shoulders. No reason could be given to account for the attack. Has used lead in painting for the past 15 years, but has had no attacks of lead colic. Lues; initial lesion at 20, secondary eruption on face, mucous patches in mouth and throat; no rheumatic pains and no loss of hair. Was treated for this at Hot Springs, Arkansas, and has had no symptoms since the secondary eruption.

Contracted gonorrhœa at 22, treated with injections and since then has had a stricture. Is in the habit of drinking two or three glasses of whiskey daily for periods of several weeks at a time, after which he will totally abstain for a corresponding period. Has never been in the habit of drinking to excess and has not used tobacco except for occasional chewing. Has usually been a healthy vigorous man up to the time of his present illness.

PRESENT ILLNESS: Patient stated that his first trouble began about two months before admission, when he noticed that he was feverish, held his head up with difficulty, lost his appetite, had severe frontal headache. This has been practically persistent since onset of trouble. He was dizzy at times. His arms and hands felt as if they were asleep. He had sensations of numbness throughout the whole body. No epistaxis. At this time patient began to have a series of chills which came on whenever he was exposed to cold and at indefinite times of the day. These chills were severe shaking rigors, and were followed by heavy sweats. Patient also had night sweats. For several weeks he has had a dry cough, at first painless but later, accompanied by painful sensations in different parts of the body; expectoration considerable, but not blood stained. Has been feverish at times since onset of disease and is constantly thirsty. No appetite, eating followed by nausea and vomiting. During this period has had definite attacks of rheumatism in knees, shoulders, elbows and hands, one knee especially involved, the other not swollen or painful.

Soon after the onset of these symptoms, patient entered the Charity Hospital, Savannah, Georgia, where he was treated for syphilis. Patient remained here for about a month when he left because he thought the mercury and iodides which he took upset his stomach. He was somewhat improved, however, and went to Richmond, Virginia, where he worked at the Soldier's Home. At this time the chills, followed by fever and sweating, became a very marked symptom of his disease and at Richmond he was treated for malaria and took large doses of quinine. He felt weak, had no appetite and was frequently feverish, had pains in different parts of the body and was utterly unfit for any active exertion. He remained in Richmond for several weeks and then came to Baltimore and was admitted to the Johns Hopkins Hospital.

On questioning, patient stated that he had had an acute attack of rheumatism (?) in the right leg and knee which came on abruptly two weeks before admission. He gave no history of attacks similar to gall stone colic and no history of attacks of jaundice at any time. Bowels were irregular, much constipated; appetite very poor. Patient has not eaten a good meal for over two months, is able to retain only soft eggs and milk. Micturition normal.

CONDITION ON ADMISSION: Complexion sallow; conjunctivæ faintly yellow; no cyanosis or dyspnoea; lips and mucous membranes of good colour; patient looks decidedly sick, is dull and slow-minded, but answers questions rationally. Tongue is slightly coated, breath very offensive; a few greyish spots on the posterior wall of the pharynx; no ulcers on membrane. Pulse slightly dicrotic, large volume, low tension. Patient has a distinctly typhoidal appearance.

LUNGS: A few fine râles at the end of inspiration in both upper lobes. Heart sounds clear; abdominal examination negative. Liver not enlarged; spleen not palpable. Abdomen soft and full, tympanitic on percussion, but not distended, no tenderness and no foreign mass to be felt; no rose spots.

The right leg is much enlarged, the tissues of the calf being swollen and indurated, the superficial temperature is elevated, there is considerable tenderness on palpation. About the middle of the calf is a ridge-like swelling, hard and sensitive, just below the line of the popliteal vein. In the popliteal space the tissues are swollen, œdematous and tender, there is much induration over the course of the popliteal artery and vein. The whole leg is swollen and œdematous pitting on pressure the circumference of right calf measuring 4 c.m. greater than the left.

COURSE OF DISEASE: The patient's temperature on admission was $102^{\circ}\frac{2}{5}$. It rose immediately to 104° and then to $105^{\circ}\frac{2}{5}$, when the patient had a hard shaking chill. It dropped again to 103 and rose to 105, and at this time the patient was covered by a most profuse perspiration. His temperature now gradually fell to $101^{\circ}\frac{1}{10}$. During the night the patient's temperature was very irregular and fell from $102^{\circ}\frac{1}{10}$ at 8 o'clock the day of admission, to normal at 10 o'clock and to 97 by the afternoon of the second day. During this time the patient looked considerably upset, the sweating was profuse, rendering a constant change of garments necessary.

There was no increase of the slight yellow tinge of the skin and conjunctivæ which had been noticed on admission and no pain in any part of the body. The spleen could not be felt, the liver was not enlarged, there was no tenderness over the gall bladder. The swelling and tenderness in the popliteal space had not increased, and if anything was slightly less than on the previous day.

The leucocyte count was 7300 on March 5th, the day of admission, and 7500 on the 6th. Fresh specimens of blood examined repeatedly for malarial parasites were absolutely negative, even though they were taken before, during and after the chills. The examination of the sputum was likewise negative. The differential blood count on March 7th, showed a great increase of polynuclear leucocytes, over 90% being of this variety.

During the afternoon of the second day the patient had a very hard shaking chill, lasting for nearly an hour; his temperature rose rapidly from 97° to 102°_{10} , after which it fluctuated for a degree or two for about four hours, when it reached 104° , and the patient had another severe shaking chill. Both chills were followed by the same profuse sweating as was noticed on the previous day. His temperature now dropped from 104° at 10 p.m. to 102° at 2 p.m. and to 96°_{10} at 4 p.m.

For the next few days patient's condition remained practically unchanged. He continued to have slight irregular elevations of temperature, but no shaking chills and no attacks of profuse sweating. The diagnosis of the convalescent stage of typhoid fever with thrombosis of the popliteal vein was made provisionally by Dr. Osler.

On the 4th day the patient had a severe pain in the left side of the chest and on auscultation there was a well marked friction rub in this area. The blood gave a positive Widal reaction in dilutions of 1—10 and 1—50. This reaction was always given by the blood of the patient from entry throughout his entire illness. On a number of occasions the reaction in dilutions of 1—100 was very rapid and perfectly characteristic.

On the 5th day the patient had another severe shaking chill, the temperature rising from 98° to 101°_{10} and to 102°_{10} , after which for half the night it remained at this point, then suddenly dropped, reaching 95° the following afternoon, a fall of nearly $7\frac{1}{2}^{\circ}$ in 14 hours. This chill was accompanied as well by profuse sweating and great constitutional discomfort.

THE URINE was turbid with a trace of albumin and a good many pus cells. Cultures gave a pure growth of typhoid bacilli, the organisms being typical, giving positive reactions on culture media and with the blood of patients suffering from typhoid fever. The administration of urotropine was begun a few days after admission with the result that after its administration the number of colonies from a given quantity of urine, gradually diminished, but at no time was the urine free from the typhoid bacilli.

The blood examination during this period was quite interesting. Although fresh specimens were examined constantly, both by day and night, and during and between the chills, there never was the slightest

evidence of the presence of any of the parasites of malarial fever although the recurrence of the chills and their irregular type led to the suspicion that we were dealing with a case of æstivo-autumnal malarial fever, and although the patient had been exposed to the different forms of malaria while living in southern countries.

The leucocyte counts were generally between 7000 and 8000 with the beginning of the chill. During the height of the fever the leucocytes would rise to 17,000 or 18,000, and frequently to 30,000, the increase being entirely due to the polymorphonuclear elements. Practically every rigor was accompanied by such a leucocytosis. The red blood count was 3,596,000, the hæmoglobin 65%.

The physical condition of the patient changed but little, the friction rub on the left side increased and the pain in this region became more marked; the spleen became palpable, very low down, the border round and soft, the area of splenic dulness much increased. The patient developed no rose spots and no jaundice and had no other symptoms of typhoid fever. The induration and swelling in the right calf in the popliteal space rapidly diminished and the patient was able to move his leg with considerable freedom. It was Dr. Osler's opinion that we were dealing with a case of typhoid fever with thrombosis.

On the 8th day at 10 p.m., the patient's temperature which had been 102°_{10} , dropped suddenly to 100, and he was attacked by a most violent rigor. The temperature rose immediately to 105°_{10} , and fell in five minutes to 96°_{10} , a drop of 9° . With this sudden fall there were most profound discomfort and general prostration; the temperature remained subnormal for only two hours, after which it rose to 99°_{10} . It fluctuated about the normal for the next two days. Blood cultures were now taken both anærobically and ærobically with negative results, but as we have said, the typhoid bacilli remained in the urine and the Widal reaction was positive.

On the 11th day the patient had another chill with a sudden rise of temperature and fall to 2° below normal, and now for several days the patient's condition remained practically unchanged. He had chills irregularly and unexpectedly at different times of the day and night, they were not, however, so violent in character nor accompanied by such great prostration; between the chills the temperature became persistently subnormal and remained so up to the day of his death.

The patient's physical condition rapidly deteriorated, weakness became more marked, mental condition decidedly unfavorable, he answered questions rationally, though it was with great difficulty he could be got to answer at all. Emaciation was profound, appetite completely lost without vomiting; there was no increase of the slight jaundice noticed on admission, in fact at times this jaundice seemed to disappear.

The blood condition was not changed, the leucocytes remaining normal between the rigors. At this time a curious attack of respiratory distress was noticed by the attendants, and the patient became very difficult to manage; he constantly complained of great pain located in the chest or abdomen, and was markedly short of breath. The examination of the chest was quite negative.

Patient became quite unruly, refused to have his temperature taken, and refused to take medicine or food; was not actually delirious, but always somewhat confused. He gradually grew worse, and his unfavorable symptoms became more marked.

On March 22nd, 17th day after admission, the patient, whose temperature had been subnormal for five days, suddenly had a shaking chill, temperature rising from 98 to 102°₁₀, afterwards dropping to 99. He had no further chills after this, his temperature persistently remaining subnormal. On the night of this day the patient was exceedingly uncomfortable, very restless, suffering greatly from dyspnoea and constantly sitting up, moving about and trying to get out of bed. He was controlled with considerably difficulty by the nurses and orderlies. The respirations were labored, both inspiration and expiration greatly prolonged. On examination there were a few moist râles over both lungs,

The jaundice now became very marked, the skin and conjunctivæ were deeply tinged and had a yellowish brown color. The edge of the liver became palpable and there was some tenderness below the right costal margin. The pulse was very soft, quite irregular and easily compressible, not accelerated.

From this time the patient rapidly went to pieces, the most marked feature being the persistent irregularity of respiration and the constant dyspnoea; the inspirations became very prolonged and the expiration correspondingly so, both were noisy and could be heard almost to the other end of the ward. The examination of the lungs remained negative. The spleen increased in size, its border was soft and round; the liver was slightly palpable. Otherwise physical examination was negative.

On the 20th day the patient was much worse, the jaundice greater with some cyanosis; respirations were of the same character, the inspirations again being very deep and accompanied by a groan. The patient became quite unconscious, not replying to questions. There was some tenderness over area of gall bladder and there seemed to be a little enlargement at this point. Radial pulse uncountable, heart beats, 21 to the quarter, respirations 25 to the minute. The blood at this time was quite negative for any foreign parasites, the leucocytes were markedly increased, the count being 25,000, many showing areas of fatty degen-

eration. The fresh blood under the microscope showed the presence in considerable numbers of long actively motile bacilli similar to the typhoid organisms. Cultures from the blood seemed to be negative, but tubes kept in the incubator for a number of days showed eventually an extremely aberrant form of the typhoid bacillus which after transplantation on to fresh culture media assumed its normal characters. The thrombus in the right leg had by this time practically disappeared.

The patient died on March 25th after a period of great restlessness and delirium. The jaundice greatly increased and a slight lateral nystagmus of the left eye developed.

During the stay of the patient in the hospital he had in all ten very profound rigors accompanied in all cases by a rise and then a sudden fall of temperature, pronounced sweating and constitutional disturbance. Besides these rigors he had almost daily attacks of chilliness and chilly sensations and at no time was he free from sweating, the skin being always moist and covered with a clammy perspiration. Cultures from this sweat failed to reveal the typhoid bacilli.

The autopsy was performed by Dr. MacCallum the day after death. The following anatomical diagnosis established. Typhoid fever with healing ulcers in the lower part of the small intestine; an acute splenic tumour with a number of infarcts; chronic aortic endocarditis; chronic diffuse interstitial nephritis; slight broncho-pneumonia; adhesions between diaphragm, left lung and spleen and small sub-pial hæmorrhages in the left frontal region in the brain.

The lesions of the intestine were limited to the region of the ileo-cæcal valve where there were a dozen nearly healed ulcers with slightly indurated bases, the ulcers being quite characteristic of typhoid fever.

The spleen was large, soft and pulpy. On its removal from the body it crumbled to pieces and was eventually removed piecemeal. The liver was not enlarged. Gall bladder not distended.

There was no pigmentation of the brain or of the viscera, either abdominal or thoracic, no lesions at all characteristic of the fevers associated with the plasmodium of Laveran were found in any part of the body. The cultures at autopsy showed a general infection by the typhoid and colon bacillus, a staphylococcus peritonitis and pleuritis.

The autopsy findings in this case demonstrated that the clinical symptoms noted were due entirely to the lesions of typhoid fever, but it is rather difficult to explain the manner of association between the symptoms and the pathological changes.

The occurrence of chills in typhoid fever is usually ascribed to the complications or accidents of the disease, especially those graver and more serious complications like cerebral thrombosis and hæmorrhages, and intestinal perforation.

Johnson, of Washington, has recently called attention to cases of typhoid fever in which rigors were present both at the onset and in the course of the fever. The case here reported may be allied to such cases, but it presents as well a number of other interesting features. The rigors were in all instances very severe. The rise and fall of temperature was most abrupt, each fluctuation being accompanied by severe shaking chills and profuse sweating. In one instance the temperature fell in five minutes from 105.4 to 96.2, a drop of over 9 degrees.

Such pronounced rigors are seen only in two conditions practically malarial fever and septicæmia.

The presence of malaria was ruled out both by the constant failure to find the parasite in the blood and the lack of any lesions at autopsy associated with this disease.

We are thus forced to conclude that we were dealing with a case of typhoid fever in which *chills* marked the whole course of the disease or with a case of typhoid septicæmia.

It is quite probable that we were dealing with both. The patient constantly stated that his illness began with chills, fever and sweating and his treatment for malaria at this time testifies to the correctness of this statement. His symptoms while in the hospital were all characteristic of septicæmia and not of an ordinary attack of typhoid.

We should thus be led to conclude that the patient originally had a mild attack of typhoid fever with a few ulcers in the intestine.

The typhoid bacilli remained in the spleen and bladder, developing and multiplying and gave rise eventually to a condition of septicæmia with the typhoid and colon bacilli as the infecting agents. This general infection was the direct cause of death.

Aside from the chills, one's attention was called particularly to several other symptoms which were unusual in typhoid.

THE JAUNDICE noticed on admission never totally disappeared. After death the body turned to a deep saffron yellow, as intense a grade of icterus being present as in obstructive jaundice. No obstruction to the flow of bile could be elicited at autopsy and no catarrh of the finer bile passages.

The jaundice was thus *hematogenous* in origin, belonging to that obscure group which is exciting so much attention from pathologists at present.

THE BLOOD showed a normal white count at all times except during the rigors when the leucocytes rose to 25,000 and 30,000. This high leucocyte count was itself quite contrary to all observations on the blood of malarial patients and suggested the infectious origin of the chills.

THE PLEURISY, the advent of which was *unassociated* with a rigor

persisted from the time of its appearance to the death of the patient. At autopsy there were plastic adhesions between the pleura, the lung and the diaphragm at the point where the pain was felt and the râles heard during life.

THE PERSPIRATION was most marked, quite as evident, indeed, as in the sudoral form of typhoid to which this case bears a little resemblance.

This sweat was highly acid in reaction, but contained no typhoid bacilli.

THE WIDAL reaction was at all times positive, both in dilutions of 1—50 and 1—100.

On admission the patient was suffering from CYSTITIS. Cultures from the urine showed the typhoid bacillus, the presence of which in reality made the diagnosis of typhoid fever seem more probable.

Young, of Baltimore, has called attention to the bladder complications in typhoid fever and has put on record several cases of typhoid cystitis. The cystitis in the present case has already been referred to by Gwynn, of Philadelphia. The typhoid bacilli never disappeared from this patient's urine, although their number was considerably diminished after the exhibition of urotropin.

THE RESPIRATORY DISTRESS was extreme for some hours before death. Dyspnoea was intense, pain in the chest severe, inspiration and expiration prolonged, the former, accompanied by a groan or grunt. This respiratory disturbance lasted for 48 hours before the fatal exit.

FRESH SPECIMENS OF BLOOD examined the last few hours before death revealed the presence in great numbers of long actively motile bacilli dodging about between the elements of the blood. Cultures from this blood at first seemed negative, but as I have stated, the transplantations made at this time, eventually gave colonies of an aberrant form of the typhoid bacillus.

FINALLY THE DIAGNOSIS OF TYPHOID FEVER WITH THROMBOSIS, reached from the positive Widal reaction and the typhoid cystitis, and the diagnosis of septicæmia resting on the observation of bacteria in the circulating blood were both confirmed by the finding at autopsy of definite typhoid ulcers and by the blood cultures at this time which showed the typhoid and colon bacilli.



